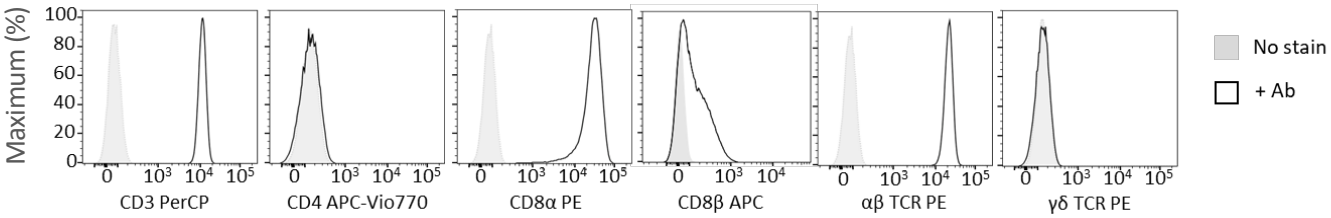
a.



b. **MC.7.G5 TCR alpha chain TRAV38.2/DV8 TRAJ31 (CDR3 underlined in bold text)**

AQTVTQSQPEMSVQEAETVTLSCTYDTSESDYYLFWYKQPPSRQMILVIRQEAYKQQNATENRFSVNFQKAAKSFSLKISD
SQLGDAAMYF**CAYRSAVNARLMF**GDGTQLVVKPNIQNDPAVYQLRDKSSDKSVCLFTDFDSQTNVSQSKDSDVYITDKC
VLDMRSMDFKSNSAVAWSNKSDFACANAFNNSIIPEDTFFPSPESS

MC.7.G5 TCR beta chain TRBV25.1 TRBJ2.3 (CDR3 underlined in bold text)

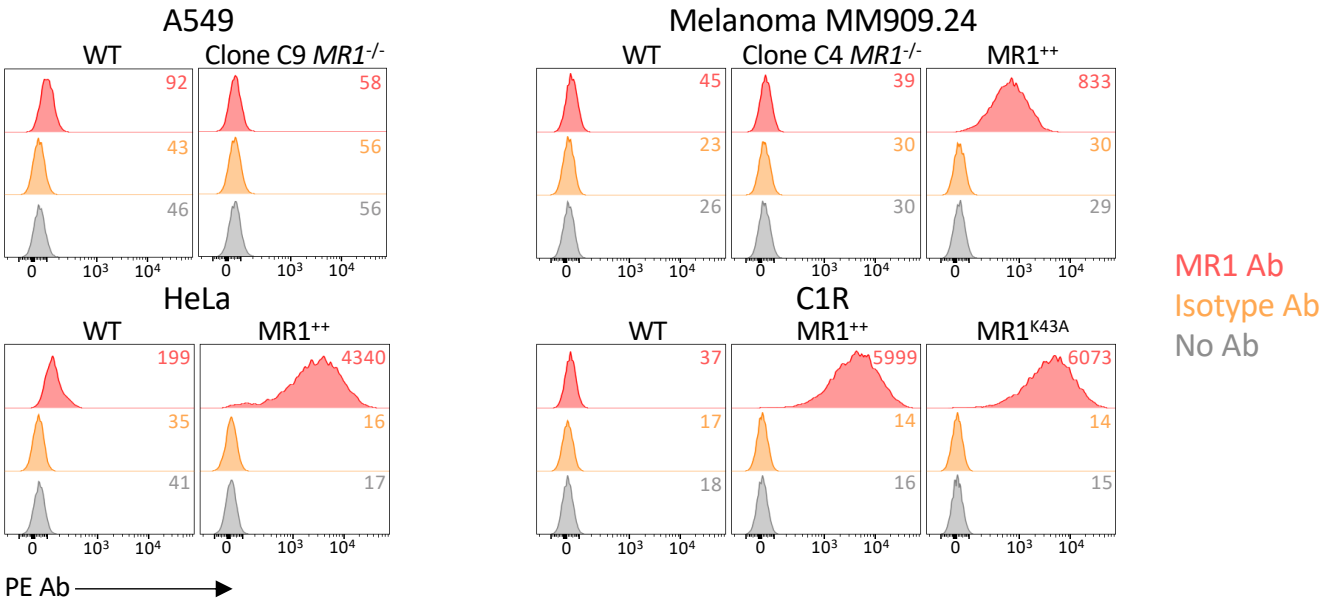
EADIYQTPRYLVIGTGKKITLECSQTMGHDKMYWYQQDPGMELHLIHYSYGVNSTEKGDLSSESTVSRIRTEHFPLTLESAR
PSHTSQYL**CASSEARGLAEFTDTQYF**GPGTRLTVLELKNVFPPEVVFEPSEAEISHTQKATLVCLATGFYPDHVELSWWVN
GKEVHSGVCTDPQPLKEQPALNDSRYALSSRLRVSATFWQDPRNHFRCQVQFYGLSENDEWTQDRAKPVTQIVSAEAWG
RA

Supplementary Figure 1. (**a**) Phenotyping of clone MC.7.G5. (**b**) T cell receptor sequence of MC.7.G5. GenBank accession codes for the cDNA sequence are MN782533 (TCRα) and MN782534 (TCR$\boldsymbol{\beta}$).

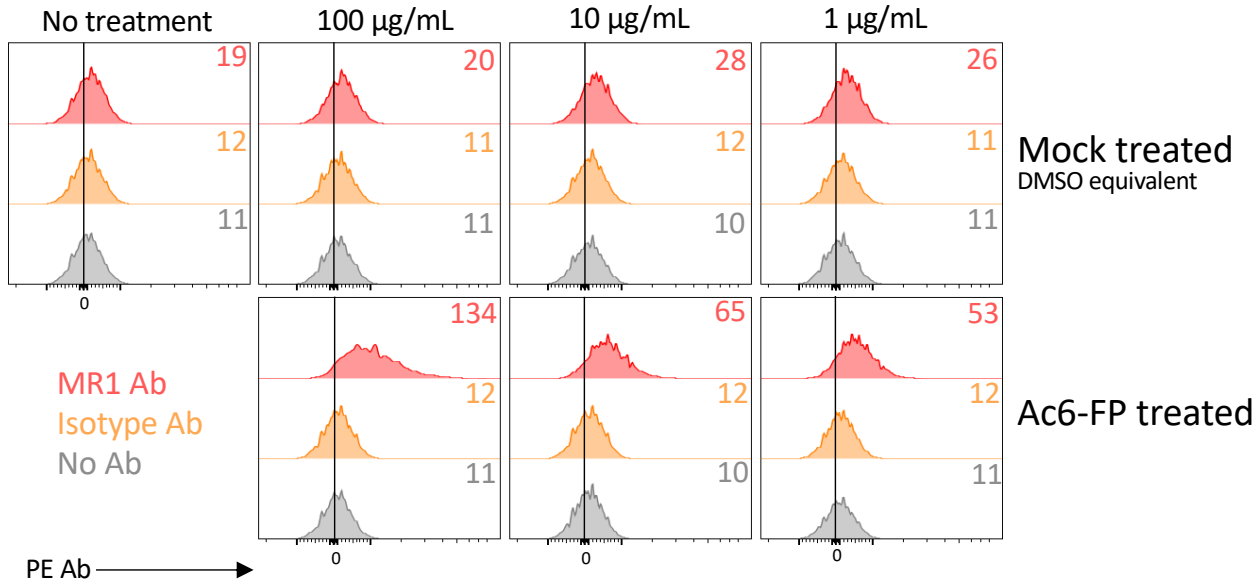
a.

Sample	DNA sequence
WT	GGACGCACTCTCTGAGATATTTTCGCCTGGGCGTTTCGGATCCCATCCATGGGGTCCCTGAATTTATTT
C4 a1	GGACGCACTCTCTGAGATATTTTCG~~CCTGGGC~~GTTTCGGATCCCATCCATGGGGTCCCTGAATTTATTT
C4 a2	GGACGCACTCTCTGAGATATTTTCGCCTG~~GG~~CGTTTCGGATCCCATCCATGGGGTCCCTGAATTTATTT

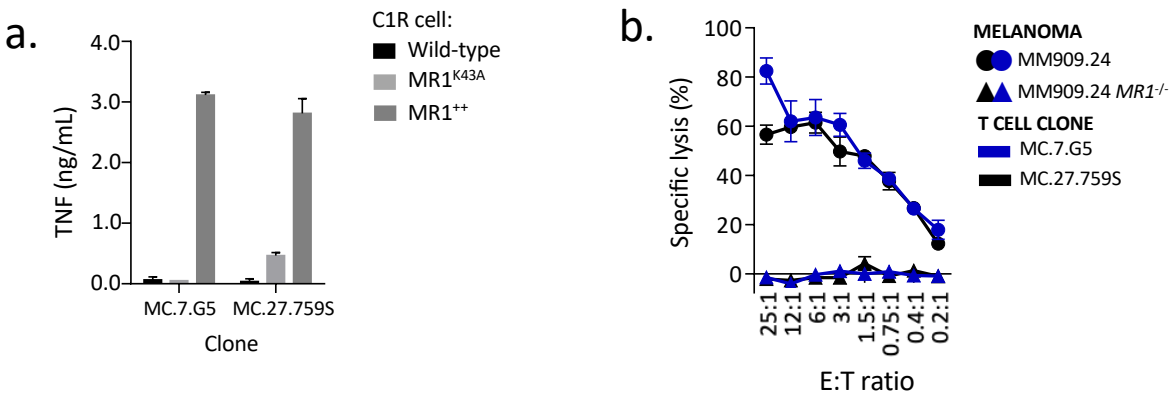
b.



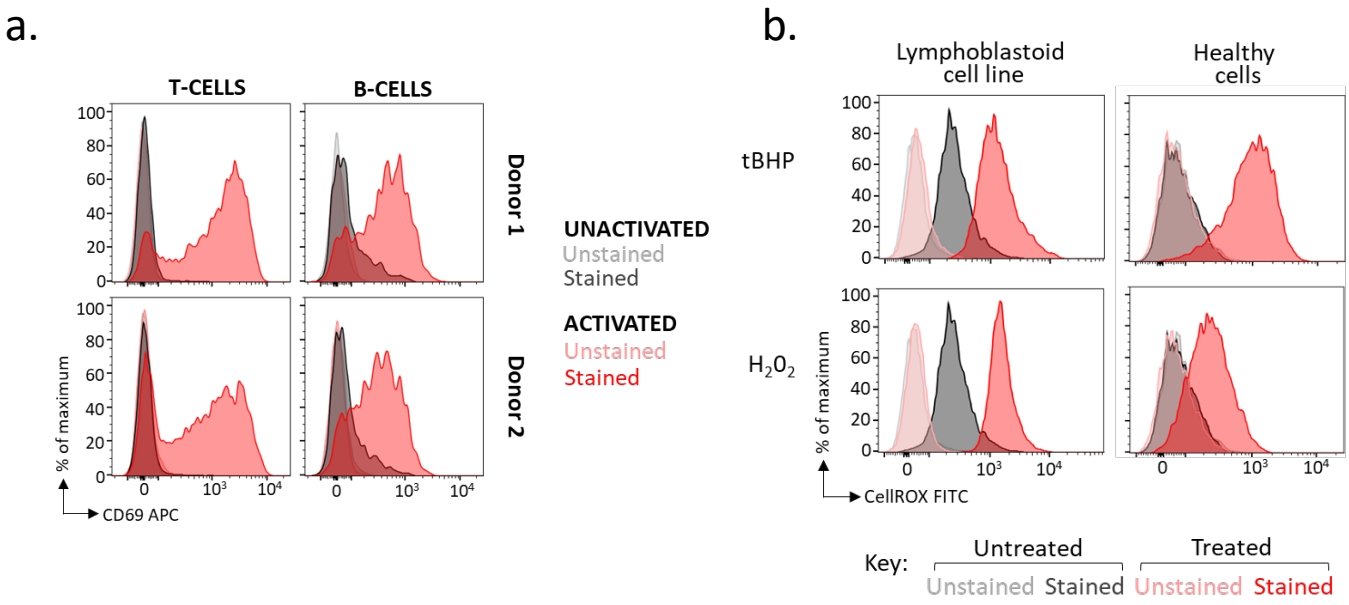
c.



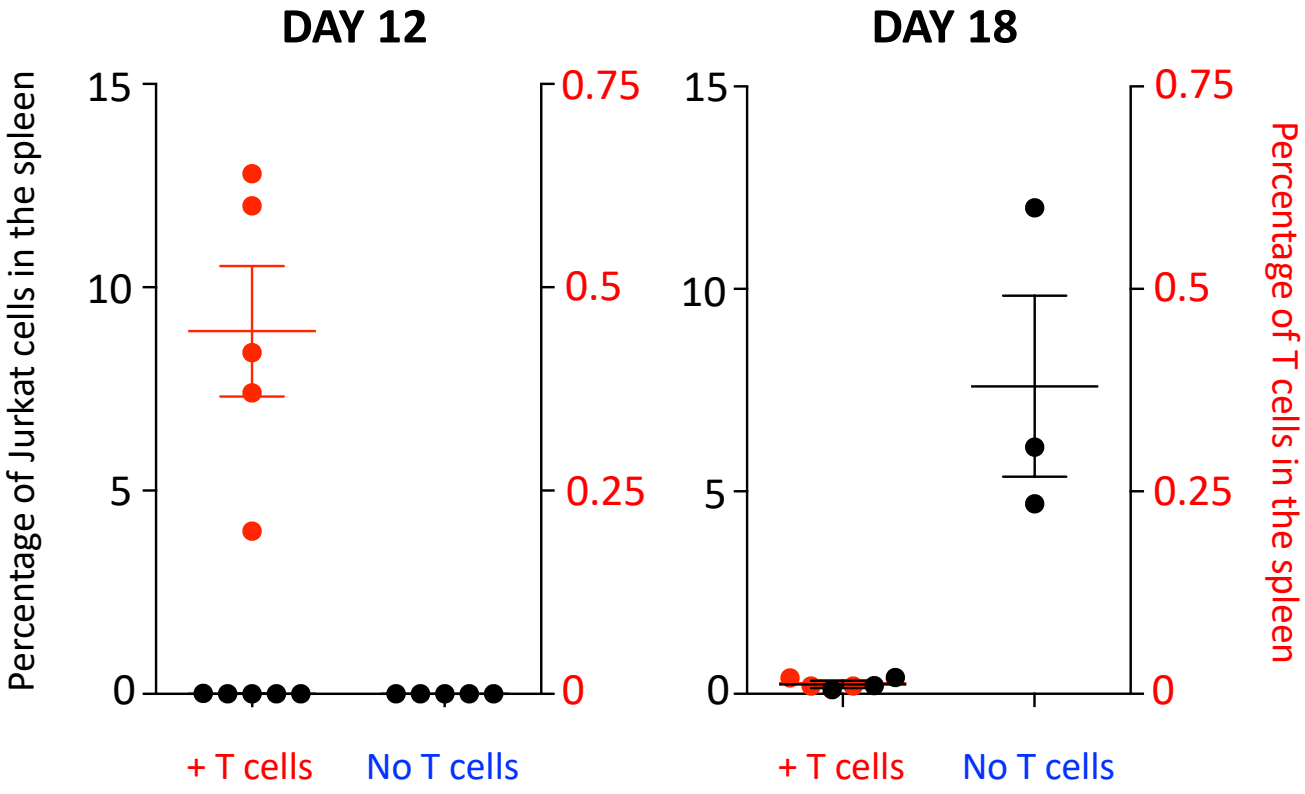
Supplementary Figure 2. (**a**) Genomic sequence of the MR1 locus of melanoma MM909.24 with MR1 CRISPR-Cas9 induced biallelic deletion in exon 2. (**b**) Antibody staining of wild-type, *MR1* gene knockout (-/-) and MR1 over-expressing (transgene ++) target cells. CIRs transduced with wild-type (++) or K43A mutant MR1. The mean fluorescence of staining is displayed. (**c**) Ac6-FP induced up-regulation of MR1 at the surface of melanoma MM909.24.



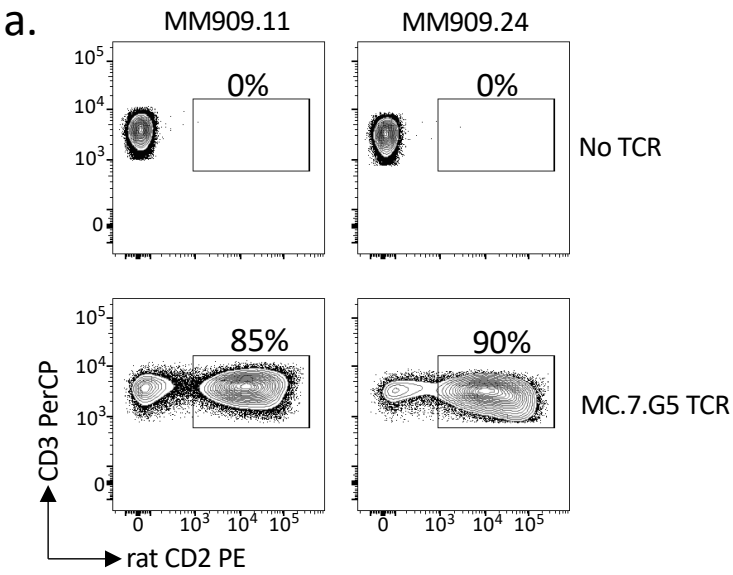
Supplementary Figure 3. MC.7.G5-like T-cell clone grown from a second donor. (**a**) Clone MC.27.759S was grown from another donor and akin to MC.7.G5 is dependent on K43 of MR1 for optimal recognition of the C1R cell line. (**d**) MC.27.759S exhibited comparable Killing of melanomas (MM909.24) to that of MC.7.G5. MR1 overexpression of WT (++) or K43A, and CRISPR/Cas9 MR1 knockout (-/-).

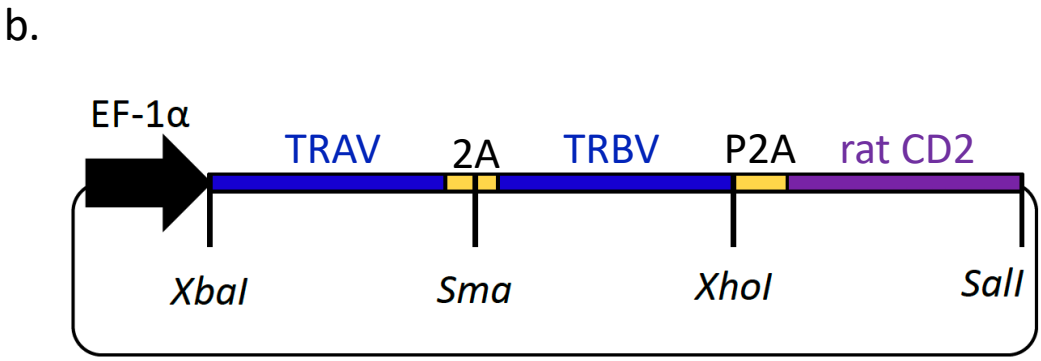


Supplementary Figure 4. Activated and stressed cells as targets of MC.7.G5. (**a**) T cells ($CD3^+$) or B cells ($CD19^+$) were purified from the PBMCs of two donors. The T cells and B cells were either left unactivated or activated overnight with either PHA or TLR9 ligand ODN2006 respectively. CD69 staining confirmed activation. The cells were used as healthy target cells for MC.7.G5. (**b**) Cells were treated for 1h with tert-Butyl hydroperoxide (tBHP) or hydrogen peroxide (H_2O_2) then stained with CellROX green reagent to detect ROS, and also VIVID to exclude dead cells. Gated on FSC vs SSC then viable cells. Untreated lymphoblastoid cell lines repeatably stained with the CellROX reagent.

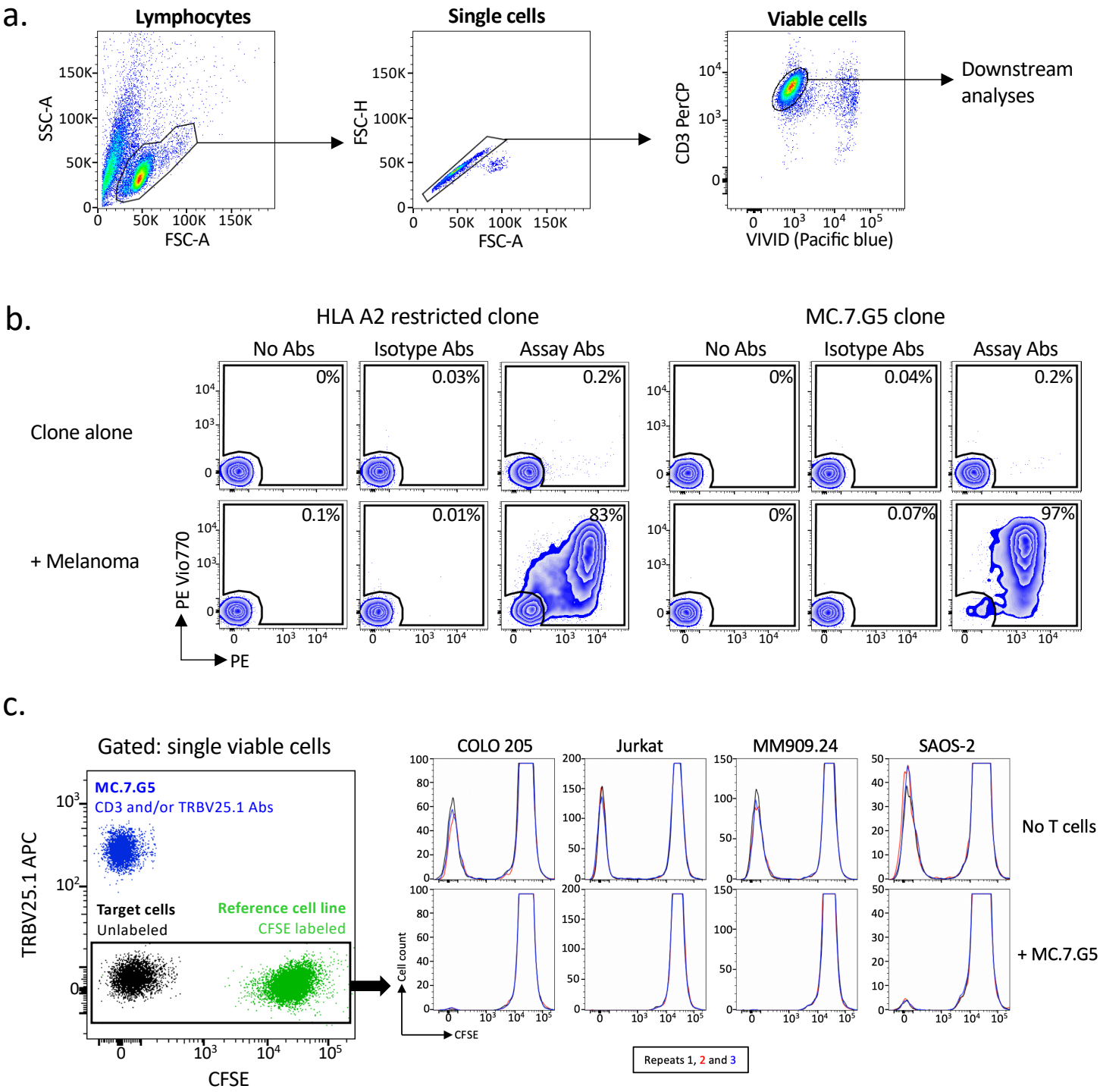


Supplementary Figure 5. MC.7.G5 prevents Jurkat cell population of the spleen. Sixteen NSG mice received 3 x10^6 Jurkat cells expressing DsRed-Express2 intravenously on day 0. Seven days post Jurkat cell transfer 8 of the mice received 3 x10^6 MC.7.G5 T cells. Mice not receiving T cells were injected intravenously with PBS. Mice were culled on day 12 or day 18 post T-cell transfer and bone marrow (main **Figure 7**) or splenocytes (this figure) harvested for analysis. Cells were stained with antibodies for human CD3, human CD8, human CD45 and mouse/human CD11b, and also for dead cells using VIVID. Gating strategy in **Supplementary Fig. 8**.

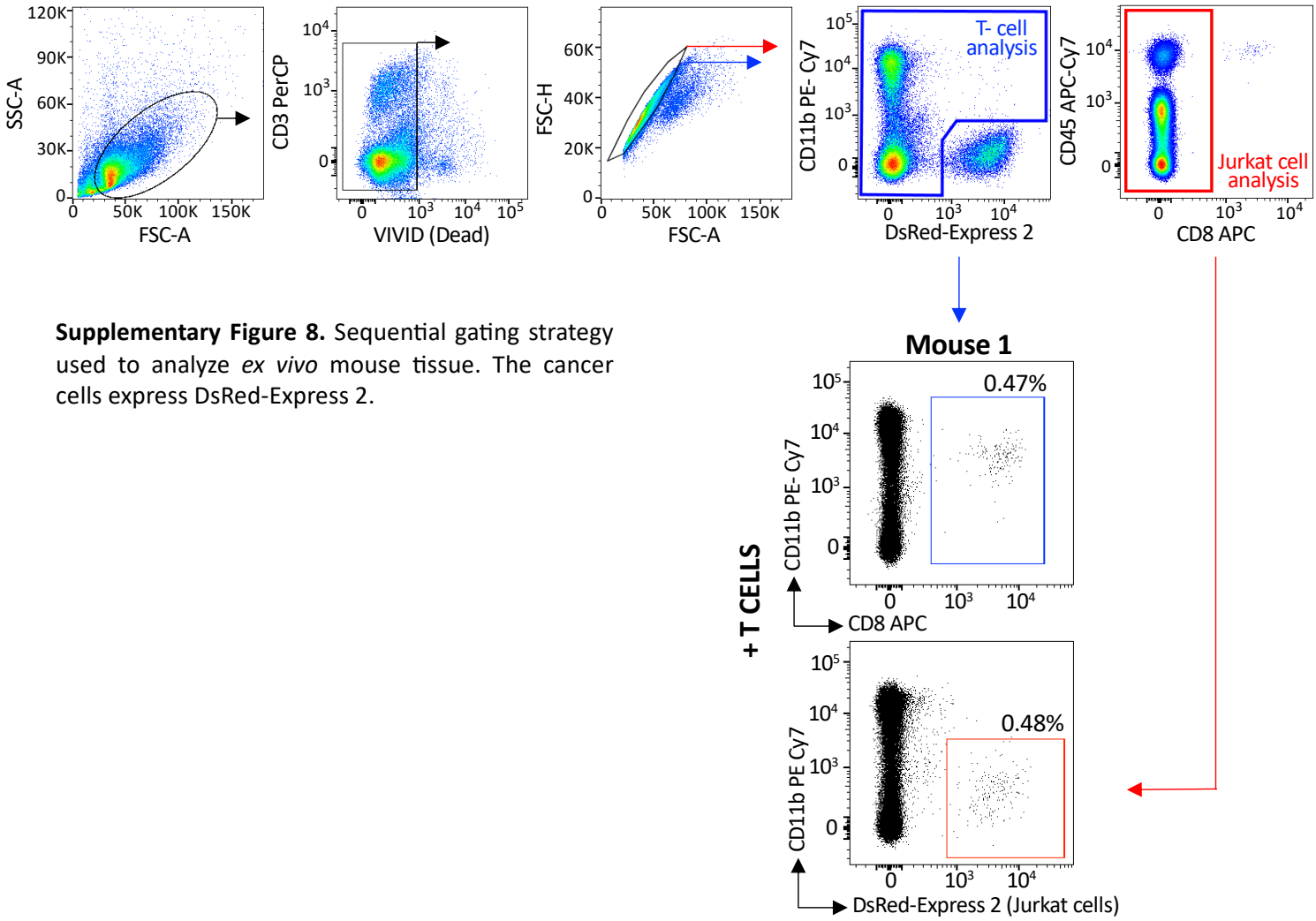




Supplementary Figure 6. (**a**) CD8 T cells transduced with a TRAV-2A-TRBV-P2A-ratCD2 lentivirus. rCD2 staining of T cells from melanoma patients MM909.11 and MM909.24, with and without transduced MC.7.G5 TCR. (**b**) Lentiviral construct (pELNS) insert for expression of the MC.7.G5 TCR.



Supplementary Figure 7. (**a**) Typical sequential gating strategy when used for experiments. (**b**) TAPI-0 assay with HLA A2 Melan A EAAGIGILTV peptide specific CD8 T-cell clone and MC.7.G5, using melanoma MM909.24 as the target cell. Performed with no TNF or CD107a Abs, isotype Abs or TNF and CD107a (assay) Abs. Gated on single viable CD8+ CD3+ cells. Zebra plot with outliers. (**c**) Exclusion of T cells during analysis of flow based killing assays. Prior gating on single and viable cancer/reference cells as shown in **a**. A larger FSC vs SSC gate was used to encompass the cancer cells.



Supplementary Figure 8. Sequential gating strategy used to analyze *ex vivo* mouse tissue. The cancer cells express DsRed-Express 2.